

In the claims:

Please amend the claims as follows:

Claims 1-8. (Cancelled)

✓ 9. (Previously presented) An isolated human antibody, or antigen-binding portion thereof, that binds to human IL-12 and dissociates from human IL-12 with a K_d of 1×10^{-10} M or less and a k_{off} rate constant of $1 \times 10^{-3} \text{ s}^{-1}$ or less, as determined by surface plasmon resonance.

✓ 10. (Previously presented) The isolated human antibody of claim 9, or an antigen-binding portion thereof, which dissociates from human IL-12 with a k_{off} rate constant of $1 \times 10^{-4} \text{ s}^{-1}$ or less.

✓ 11. (Previously presented) The isolated human antibody of claim 9, or an antigen-binding portion thereof, which dissociates from human IL-12 with a k_{off} rate constant of $1 \times 10^{-5} \text{ s}^{-1}$ or less.

✓ 12. (Previously presented) The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-9} M or less.

✓ 13. (Previously presented) The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-10} M or less.

✓ 14. (Previously presented) The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-11} M or less.

Claims 15-40. (Cancelled)

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41. (Original) An isolated human antibody, or an antigen-binding portion thereof, which

- a) inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC₅₀ of 1 x 10⁻⁹ M or less;
- b) has a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 25; and
- c) has a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 26.

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42. (Original) 16 The isolated human antibody, or an antigen-binding portion thereof, of claim 41 which further has a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO: 27; and a light chain CDR2 comprising the amino acid sequence of SEQ ID NO: 28.

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43. (Original) 16 The isolated human antibody, or an antigen-binding portion thereof, of claim 41 which further has a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO: 29; and a light chain CDR1 comprising the amino acid sequence of SEQ ID NO: 30.

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44. (Original) An isolated human antibody, or an antigen-binding portion thereof, having a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 31, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 32.

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45. (Original) The isolated human antibody of claim 44, comprising a heavy chain constant region selected from the group consisting of IgG1, IgG2, IgG3, IgG4, IgM, IgA and IgE constant regions.

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46. (Original) The isolated human antibody of claim 45, wherein the antibody heavy chain constant region is IgG1.

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47. (Original) The isolated human antibody of claim 44, which is a Fab fragment.

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48. (Original) The isolated human antibody of claim 44, which is a F(ab')₂ fragment.

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49. (Original) The isolated human antibody of claim *44*, which is a single chain Fv fragment.

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Claims 50-87. (Cancelled)

b 4 *88.* (Previously presented) A pharmaceutical composition comprising the antibody or an antigen binding portion thereof, of claim *9, 41, 44, 151, 153, 164, 167, 168, 172, 183, or 184*, and a pharmaceutically acceptable carrier. *162) 27 29 41 44*
45 48 50 51

Claims 89-90 (Cancelled)

b 5 *89.* (Previously presented) The pharmaceutical composition of claim *88*, further comprising an additional therapeutic agent selected from the group consisting of budesonide, corticosteroids, cyclosporin, sulfasalazine, aminosalicylates, 6-mercaptopurine, azathioprine, metronidazole, mesalamine, olsalazine, balsalazide, antioxidants, antibodies to IL-1 receptor, anti-IL-1 β monoclonal antibodies, anti-IL-6 monoclonal antibodies, pyridinyl-imidazole compounds, anti-TNF antibodies, or fragments thereof, and anti-LT antibodies.

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Claims 92-141. (Cancelled)

b 142. (Previously presented) The isolated human antibody, or antigen-binding portion thereof, of claim *9*, which is a recombinant antibody, or antigen-binding portion thereof.

7 *143.* (Previously presented) The isolated human antibody of any one of claims *9* to *141*, wherein the antibody is a neutralizing antibody.

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144. (Previously presented) The neutralizing antibody of claim *143*, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* phytohemagglutinin blast proliferation assay (PHA assay) with an IC₅₀ of 1 x 10⁻⁷ M or less.

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145. (Previously presented) The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC₅₀ of 1×10^{-8} M or less

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146. (Previously presented) The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC₅₀ of 1×10^{-10} M or less.

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147. (Previously presented) The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC₅₀ of 1×10^{-11} M or less.

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148. (Previously presented) The neutralizing antibody of claim 143, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC₅₀ of 5×10^{-12} M or less.

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149. (Previously presented) 16 The isolated human antibody, or antigen-binding portion thereof, of claim 41, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC₅₀ of 1×10^{-10} M or less.

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150. (Previously presented) 16 The isolated human antibody, or antigen-binding portion thereof, of claim 41, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC₅₀ of 1×10^{-11} M or less.

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151. (Previously presented) An isolated human antibody, or an antigen-binding portion thereof, which dissociates from human IL-12 with a K_d of 1×10^{-10} M or less and binds to an epitope on the p40 subunit of human IL-12.

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152. (Previously presented) The isolated human antibody of claim 151, which neutralizes the activity of human IL-12.

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153. (Currently amended) A neutralizing isolated human antibody, or antigen-binding portion thereof, that binds to human IL-12 and dissociates from human IL-12 with a k_{off} rate constant of $1 \times 10^{-2} s^{-1} + * 10^{-3} s^{-1}$ or less, as determined by surface plasmon resonance.

30 ^{154.} (Currently amended) The neutralizing isolated human antibody of claim ^{153,} or an antigen-binding portion thereof, which dissociates from human IL-12 with a ²⁹ k_{off} rate constant of $1 \times 10^{-4} s^{-1}$ or less.

31 ^{155.} (Previously presented) The neutralizing isolated human antibody of claim ^{153,} or an antigen-binding portion thereof, which dissociates from human IL-12 with a k_{off} rate constant of $1 \times 10^{-5} s^{-1}$ or less.

33 ^{156.} (Currently amended) The neutralizing isolated human antibody of any one of claims ^{153 to 155 and 207,} which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of $1 \times 10^{-7} M$ or less.

34 ^{157.} (Currently amended) The neutralizing isolated human antibody of any one of claims ^{153 to 155 and 207,} or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of $1 \times 10^{-8} M$ or less.

35 ^{158.} (Currently amended) ³² The neutralizing isolated human antibody of any one of claims ^{153 to 155 and 207,} or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of $1 \times 10^{-9} M$ or less.

36 ^{159.} (Currently amended) ³² The neutralizing isolated human antibody of any one of claims ^{153 to 155 and 207,} or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of $1 \times 10^{-10} M$ or less.

37 ^{160.} (Currently amended) ³² The neutralizing isolated human antibody of any one of claims ^{153 to 155 and 207,} or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of $1 \times 10^{-11} M$ or less.

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161. (Currently amended) ³ ₂ The neutralizing isolated human antibody of any one of claims 153 to 155 and 207, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC₅₀ of 1×10^{-10} M or less.

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162. (Currently amended) ³ ₂ The neutralizing isolated human antibody of any one of claims 153 to 155 and 207, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC₅₀ of 1×10^{-11} M or less.

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163. (Currently amended) ³ ₂ The neutralizing isolated human antibody of any one of claims 153 to 155 and 207, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC₅₀ of 5×10^{-12} M or less.

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164. (Previously presented) An isolated human antibody, or an antigen-binding portion thereof, which

- a) dissociates from human IL-12 with a k_{off} rate constant of $1 \times 10^{-3} s^{-1}$ or less, as determined by surface plasmon resonance;
- b) has a heavy chain CDR3 comprising the amino acid sequence of SEQ ID NO: 25; and
- c) has a light chain CDR3 comprising the amino acid sequence of SEQ ID NO: 26.

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165. (Previously presented) The isolated human antibody of claim 164, or an antigen-binding portion thereof, which dissociates from human IL-12 with a k_{off} rate constant of $1 \times 10^{-4} s^{-1}$ or less.

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166. (Previously presented) The isolated human antibody of claim 164, or an antigen-binding portion thereof, which dissociates from human IL-12 with a k_{off} rate constant of $1 \times 10^{-5} s^{-1}$ or less.

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167. (Previously presented) An isolated human antibody, or antigen-binding portion thereof, that binds to human IL-12 and comprises:
a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 26; and
a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 25.

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168. (Previously presented) An isolated human antibody, or an antigen-binding portion thereof, with a light chain variable region (LCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 26, and with a heavy chain variable region (HCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 25.

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169. (Previously presented) *us* The isolated human antibody, or an antigen-binding portion thereof, of claim 168, wherein the LCVR further has a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 28 and the HCVR further has a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 27.

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170. (Previously presented) *us* The isolated human antibody, or an antigen-binding portion thereof, of claim 169, wherein the LCVR further has CDR1 domain comprising the amino acid sequence of SEQ ID NO: 30 and the HCVR has a CDR1 domain comprising the amino acid sequence of SEQ ID NO: 29.

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171. (Previously presented) A pharmaceutical composition comprising an antibody or an antigen binding portion thereof, and a pharmaceutically acceptable carrier, wherein the antibody comprises:
a light chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 26; and
a heavy chain CDR3 domain comprising the amino acid sequence of SEQ ID NO: 25.

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172. (Previously presented) An isolated human antibody that binds human IL-12 and is the antibody J695, or an antigen binding portion thereof.

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173. (Previously presented) *us* A pharmaceutical composition comprising the isolated human antibody of claim 172 and a pharmaceutically acceptable carrier.

Claims 174-182. (Canceled)

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183. (Previously presented) An isolated human antibody, or antigen-binding portion thereof, that binds to human IL-12 and dissociates from human IL-12 with a K_d of 1.34×10^{-10} M or less, and neutralizes human IL-12.

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184. (Previously presented) The isolated human antibody of claim 183, or an antigen-binding portion thereof, which dissociates from human IL-12 with a K_d of 9.74×10^{-11} M or less.

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185. (Previously presented) The isolated human antibody, or antigen-binding portion thereof, of claims 183 or 184, which is a recombinant antibody, or antigen-binding portion thereof.
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186. (Previously presented) The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-7} M or less.

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187. (Previously presented) The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-8} M or less.

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188. (Previously presented) The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-9} M or less.

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189. (Previously presented) The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-10} M or less.

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190. (Previously presented) The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits phytohemagglutinin blast proliferation in an *in vitro* PHA assay with an IC_{50} of 1×10^{-11} M or less.

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191. (Previously presented) The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC₅₀ of 1 $\times 10^{-10}$ M or less.

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192. (Previously presented) The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC₅₀ of 1 $\times 10^{-11}$ M or less.

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193. (Previously presented) The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits human IFN γ production with an IC₅₀ of 5 $\times 10^{-12}$ M or less.

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194. (Previously presented) The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits IL-12 binding to its receptor in an IL-12 receptor binding assay (RBA) with an IC₅₀ of 1 $\times 10^{-9}$ M or less.

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195. (Previously presented) The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits IL-12 binding to its receptor in an IL-12 receptor binding assay (RBA) with an IC₅₀ of 1 $\times 10^{-10}$ M or less.

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196. (Previously presented) The isolated human antibody of claim 185, or an antigen-binding portion thereof, which inhibits IL-12 binding to its receptor in an IL-12 receptor binding assay (RBA) with an IC₅₀ of 1 $\times 10^{-11}$ M or less.

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197. (Previously presented) The pharmaceutical composition of claim 88, further comprising an additional therapeutic agent selected from the group consisting of anti-IL-1 antibodies, anti-IL-2 antibodies, anti-IL-6 antibodies, anti-IL-7 antibodies, anti-IL-8 antibodies, anti-IL-15 antibodies, anti-IL-16 antibodies, anti-IL-18 antibodies, anti-EMAP-II antibodies, anti-GM-CSF antibodies, anti-FGF antibodies, anti-PDGF antibodies, anti-CD2 antibodies, anti-CD3 antibodies, anti-CD4 antibodies, anti-CD8 antibodies, anti-CD25 antibodies, anti-CD28 antibodies, anti-CD30 antibodies, anti-CD40 antibodies, anti-CD45 antibodies, anti-CD69 antibodies, anti-CD80 (B7.1) antibodies, anti-CD86 (B7.2) antibodies, and anti-CD90 antibodies.

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b7C 198. (Previously presented) The pharmaceutical composition of claim 88, further comprising an additional therapeutic agent selected from the group consisting of methotrexate, FK506, rapamycin, mycophenolate mofetil, leflunomide, non-steroidal anti-inflammatory drugs (NSAIDs), ibuprofen, prednisolone, 6-mercaptopurines, soluble p55 TNF receptor, soluble p75 TNF receptor, sIL-1RI, sIL-1RII, sIL-6R, sIL-13, antiinflammatory cytokines, IL-4, IL-10, IL-11, IL-13, TGF β , Vx740, anti-P7s, p-selectin glycoprotein ligand (PSGL), p75TNFR IgG (EnbrelTM), p55TNFR IgG (LenerceptTM), pyridinyl-imidazole compounds, anti-gp39 antibodies, anti-CD40L antibodies, methotrexate, cytokine suppressive anti-inflammatory drugs (CSAIDs), leflunomide, MP, mesalazine, chloroquine/hydroxychloroquine, penicillamine, aurothiomalate, cochicine, salbutamol, terbutaline, salmeterol, theophylline, aminophylline, cromoglycate, nedocromil, ketotifen, ipratropium, and oxitropium.

b7C 199. (Previously presented) The pharmaceutical composition of claim 88, further comprising an additional therapeutic agent selected from the group consisting of anti-IRAK antibodies, anti-NIK antibodies, anti-IKK antibodies, anti-p38 antibodies, D2E7, cA2 (RemicadeTM), CDP 571, 5-aminosalicylic acid, TNFR-Ig constructs, dexamethasone, aminosalicylic acid, IL-1ra, methylprednisolone, cyclophosphamide, methotrexate, 4-aminopyridine, tizanidine, interferon- β 1a (AvonexTM), interferon- β 1b (BetaseronTM), Copolymer 1 (Cop-1; CopaxoneTM), hyperbaric oxygen, clabribine, anti-EMAP-II antibodies, IFN β 1a, IFN β 1b, and IL-1.

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200. ((Previously presented)) A pharmaceutical composition comprising the antibody or an antigen binding portion thereof of claim 143, and a pharmaceutically acceptable carrier.

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201. (Previously presented) The pharmaceutical composition of claim 200, further comprising an additional therapeutic agent selected from the group consisting of budesonide, corticosteroids, cyclosporin, sulfasalazine, aminosalicylates, 6-mercaptopurine, azathioprine, metronidazole, mesalamine, olsalazine, balsalazide, antioxidants, antibodies to IL-1 receptor, anti-IL-1 β monoclonal antibodies, anti-IL-6

monoclonal antibodies, pyridinyl-imidazole compounds, anti-TNF antibodies, or fragments thereof, and anti-LT antibodies.

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202. (Previously presented) The pharmaceutical composition of claim 200, further comprising an additional therapeutic agent selected from the group consisting of anti-IL-1 antibodies, anti-IL-2 antibodies, anti-IL-6 antibodies, anti-IL-7 antibodies, anti-IL-8 antibodies, anti-IL-15 antibodies, anti-IL-16 antibodies, anti-IL-18 antibodies, anti-EMAP-II antibodies, anti-GM-CSF antibodies, anti-FGF antibodies, anti-PDGF antibodies, anti-CD2 antibodies, anti-CD3 antibodies, anti-CD4 antibodies, anti-CD8 antibodies, anti-CD25 antibodies, anti-CD28 antibodies, anti-CD30 antibodies, anti-CD40 antibodies, anti-CD45 antibodies, anti-CD69 antibodies, anti-CD80 (B7.1) antibodies, anti-CD86 (B7.2) antibodies, and anti-CD90 antibodies.

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203. (Previously presented) The pharmaceutical composition of claim 200, further comprising an additional therapeutic agent selected from the group consisting of methotrexate, FK506, rapamycin, mycophenolate mofetil, leflunomide, non-steroidal anti-inflammatory drugs (NSAIDs), ibuprofen, prednisolone, 6-mercaptopurines, soluble p55 TNF receptor, soluble p75 TNF receptor, sIL-1RI, sIL-1RII, sIL-6R, sIL-13, antiinflammatory cytokines, IL-4, IL-10, IL-11, IL-13, TGF β , Vx740, anti-P7s, p-selectin glycoprotein ligand (PSGL), p75TNFR IgG (EnbrelTM), p55TNFR IgG (LenerceptTM), pyridinyl-imidazole compounds, anti-gp39 antibodies, anti-CD40L antibodies, methotrexate, cytokine suppressive anti-inflammatory drugs (CSAIDs), leflunomide, MP, mesalazine, chloroquine/hydroxychloroquine, penicillamine, aurothiomalate, cochicine, salbutamol, terbutaline, salmeterol, theophylline, aminophylline, cromoglycate, nedocromil, ketotifen, ipratropium, and oxitropium.

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204. (Previously presented) The pharmaceutical composition of claim 200, further comprising an additional therapeutic agent selected from the group consisting of anti-IRAK antibodies, anti-NIK antibodies, anti-IKK antibodies, anti-p38 antibodies, D2E7, cA2 (RemicadeTM), CDP 571, S-aminosalicylic acid, TNFR-Ig constructs, dexamethasone, aminosalicylic acid, IL-1ra, methylprednisolone, cyclophosphamide, methotrexate, 4-aminopyridine, tizanidine, interferon- β 1a (AvonexTM), interferon- β 1b

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(BeraseronTM), Copolymer I (Cop-I; CopaxoneTM), hyperbaric oxygen, clabribine, anti-EMAP-II antibodies, IFN β 1a, IFN β 1b, and IL-1.

✓ 205. (Previously presented) The isolated human antibody of claim 9, or an antigen-binding portion thereof, that binds to human IL-12 and dissociates from human IL-12 with a K_d of 1.34×10^{-10} M or less.

✓ 206. (Previously presented) The isolated human antibody of claim 9, or an antigen-binding portion thereof, that binds to human IL-12 and dissociates from human IL-12 with a K_d of 9.74×10^{-11} M or less.

✓ 207. (New) The neutralizing isolated human antibody of claim 153, or an antigen-binding portion thereof, which dissociates from human IL-12 with a k_{off} rate constant of $1 \times 10^{-3} s^{-1}$ or less.

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